Case Reports in Neurology

Case Rep Neurol 2017;9:293–298

DOI: 10.1159/000484682
Published online: December 18, 2017

Case Report

Recurrent Stroke in a Young Woman with a Single Pulmonary Arteriovenous Fistula: An Unusual Association

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Keywords
Stroke · Extracardiac shunt · Fistula · Pulmonary arteriovenous fistula

Abstract
Introduction: Cryptogenic stroke is present in about 40% of ischemic stroke patients. Extracardiac shunt related to pulmonary arteriovenous fistula (PAVF) could be a rare potential risk factor for embolic stroke. Most PAVFs are multiple, congenital, and associated with hereditary conditions. On the other hand, isolated PAVFs are rare conditions and an uncommon cause of cryptogenic stoke. ***Case Report:*** We describe a case of a young woman without history of respiratory diseases or vascular risk factors, who presented with acute onset of transitory aphasia and right hemiplegia. She had a history of a transient ischemic attack, 3 years before, and migraine headaches. Brain MRI showed an acute cortical ischemic lesion and a chronic ischemic lesion. Diagnostic workup with transcranial Doppler ultrasonography revealed a significant right-to-left shunt with curtain pattern, and echocardiogram did not show structural abnormalities. An isolated small PAVF was diagnosed on pulmonary angiogram. Despite the rare association between isolated small PAVF and stroke, we decided to treat it with coil embolization because of recurrence of stroke, cortical lesions suggestive of embolic source, significant right-left shunt, and risk of future complications. ***Conclusions:*** This case highlights the importance of search, identification, and interpretation of causes of

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cryptogenic strokes to better choose therapy to reduce the stroke recurrence risk. Although unusual, PAVF detection is a treatable cause of stroke and the therapeutic decisions should take into account the characteristics of the PAVF and the degree of suspicion regarding the cause-effect relationship between PAVF and stroke.

Introduction

Cryptogenic stroke occurs in about 40% of ischemic stroke patients, and the identification of its pathophysiological mechanism remains a challenge [1]. The paradoxical embolism through a patent foramen ovale is a potential mechanism in young patients [2]. However, extracardiac shunting and pulmonary arteriovenous fistula (PAVF) can also be associated with paradoxical embolism and ischemic stroke. PAVFs are rare vascular anomalies in which an abnormal communication between the pulmonary vein and artery result in a high-flow and low-resistant right-to-left shunt. Most of them (about 80%) are congenital and are often associated with Osler-Weber-Rendu disease [3].

Herein we report a case of a single PAVF in an adult female, without Osler-Weber-Rendu disease, in which the first clinical manifestation was a recurrent stroke.

Clinical Case

A 46-year-old woman was brought to the emergency department of our hospital because of transitory right hemiplegia and language disturbance of sudden onset.

On admission, she was afebrile with normal vital signs and general examination. No mucocutaneous alterations were detected. Neurologic examination revealed a decrease of pinprick sensation in the right members. Her past medical history was notable for migraine and an episode of numbness of the left limbs lasting more than 2 days, 3 years before, for which she never sought medical attention. She did not smoke, consume use alcohol, or use illicit drugs. There was no history of other vascular risk factors. She has first-degree relatives with breast, ovarian, and uterine cancer.

The patient underwent DWI-MRI (Fig. 1a) that showed several hyperintense cortical lesions in the left middle cerebral artery distribution with low apparent diffusion coefficient values. FLAIR (Fig. 1b) revealed an old ischemic lesion in the right middle cerebral artery distribution. Cervical and brain MR angiography sequences excluded carotid or intracranial arterial stenosis.

Blood gas analysis was normal. Extensive laboratory with assessment of thrombophilia, including antithrombin III, C protein, S protein, factor VIII, antiphospholipid antibody, lupus anticoagulant, factor V Leiden, and homocysteine was normal. Thyroid-stimulating hormone, free T4, ANCAs, SSA, SSB, anti-nuclear antibody, rheumatoid factor, C3, C4, and Lyme serology were within normal limits.

No cardiac rhythm abnormalities were noted on 24-hour Holter monitoring and a duplex ultrasound of the carotid vessels did not reveal any abnormalities. A transthoracic and transesophageal echocardiogram had no evidence for patent foramen ovale, congenital cardiac defects, patent ductus arteriosus, pulmonary hypertension, or aortic arch plaque. A contrast-enhanced transcranial Doppler ultrasonography (CE-TCD) (Fig. 1d) was performed and showed late passage of a higher number of microembolic signals with a curtain pattern in the middle cerebral artery, compatible with a significant right-to-left shunt.

Given the right-to-left shunt, in absence of cardiac structural anomalies, we considered the hypothesis of pulmonary shunting. Thus, the patient underwent thoracic 3D CT angiography (Fig. 2a) that showed a single PAVF in the lateral segment of the middle lobe. The feeding artery had an average diameter of about 1.7 mm, the nidus measured 3 × 1.4 cm, and the drainage vein about 1.9 mm.

Lower extremity venous duplex ultrasound and an abdominal-pelvic-lower limbs venous-phase CT did not revealed occult venous thrombosis. The pursuit for occult neoplasm was unremarkable.

On the following days, the Interventional Radiology Team performed a selective right pulmonary arterial angiography and proceeded to selective embolization with microcoils of the PAVF. Technical success was achieved in the control angiography (Fig. 2b, c). The patient was discharged the next morning. Her repeat TCD, 2 months later, was normal, with resolution of the right-to-left shunt (Fig. 3a, b).

Discussion

The available literature on PAVFs and ischemic stroke is limited with little information about the proportion of ischemic strokes that are due to pulmonary PAVFs. However, it is well known that the prevalence of stroke is high in cases with multiple PAVFs (reaches 60%) and very rare in patients with single PAVF [4]. Therefore, PAVFs must be remembered as an important cause of stroke, especially in young patients with unknown etiology during the workup.

Even though the majority of PAVFs manifest themselves by respiratory complaints, usually in the third or the forth decade, neurological conditions such as ischemic stroke, transient ischemic attack, intracerebral hemorrhage, seizure, or cerebral abscess can be the first clinical manifestation [5].

Our case had neither a history suggestive of acquired causes nor any symptoms nor family history of Rendu-Osler-Weber disease. Hence, we assume that her PAVF might be congenital, manifested in adulthood with a recurrent stroke.

It is generally accepted that there is a direct correlation between the severity of neurological symptoms and the size and number of the PAVFs. It is usually accepted that multiple PAVFs and PAVFs with a diameter >2 cm or with a feeding artery >3 mm are associated with an increased risk of neurological complications [5] and a single PAVF or a PAVF with a diameter <2 cm are usually not responsible for any significant symptoms [3]. However, those 2 criteria, the size and number of PAVFs, do not explain the occurrence of several clinical manifestations and, probably, other factors might be involved. Indeed, we found very few cases reported of cryptogenic stroke in patients with single and smaller PAVFs [6–10]. So the treatment applied in these situations covers not only the PAVF with a diameter >2 cm or with a feeding artery >3 mm, but also all symptomatic patients independently of PAVF size and number [11–13].

Although no emboli or prothrombotic factors were found, and despite being a single PAVF, we decided to treat the patient with embolotherapy for several reasons. First, the neuroimaging features with acute and chronic superficial hemispheric infarcts were suggestive of an embolic source. Second, TCD was highly suggestive of significant right-left shunt, so we considered the patient to have a non-negligible risk for future complications. Furthermore, the possible growth of PAVF during the next years would increase that risk, especially the risk of new neurological complications [3].

A learning point from this case is the importance of search, identification, and interpretation of causes of cryptogenic strokes to better decide on the correct therapy to reduce the stroke recurrence risk. Although unusual, PAVF detection is of the utmost importance since it is a treatable cause of stroke. The therapeutic decisions should take into account not only the characteristics of the PAVF, but also the degree of suspicion regarding the cause-effect relationship between PAVF and stroke. For that, the clinical history and the stroke details are of extreme importance.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that they have no conflict of interest.

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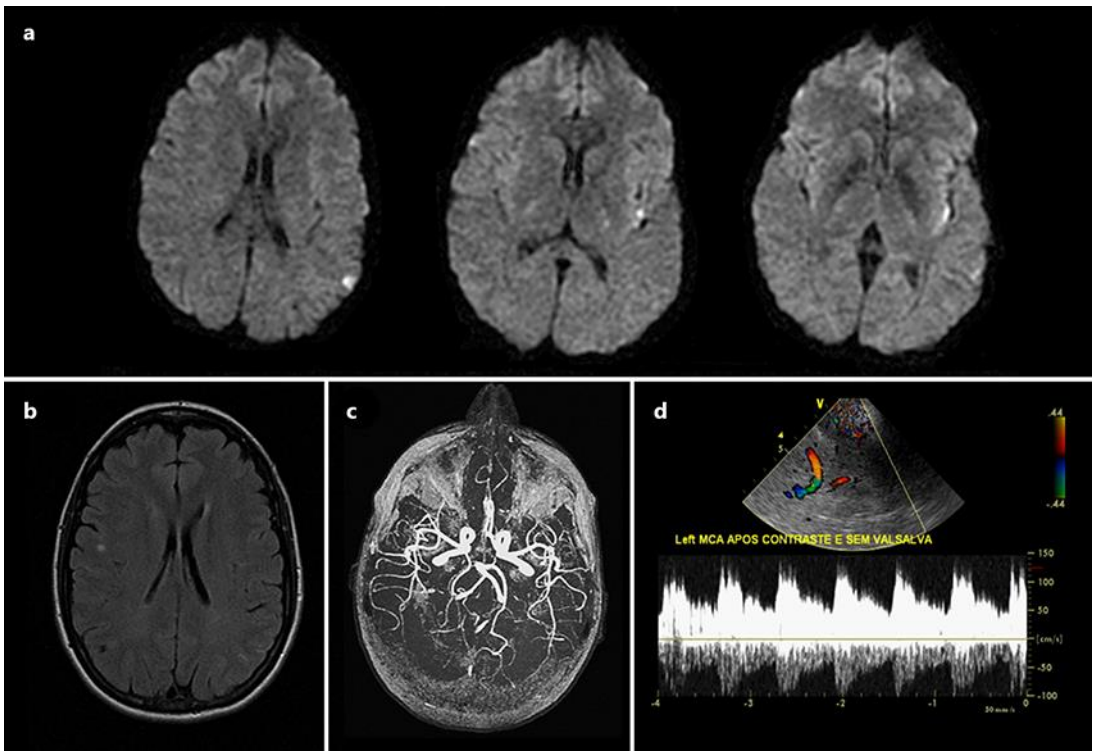

Fig. 1. Brain MRI and TCD. **a** DWI-MRI shows small hyperintense cortical lesions in the temporal and insular regions. **b** FLAIR-MRI identifies a hyperintense cortical-subcortical lesion in the parietal region, without hyperintensity on DWI. **c** MR angiogram shows no abnormalities in the neck and the cerebral blood vessel. **d** CE-TCD (microbubble contrast agent) demonstrates a higher number of microembolic signals with a curtain pattern, at rest.

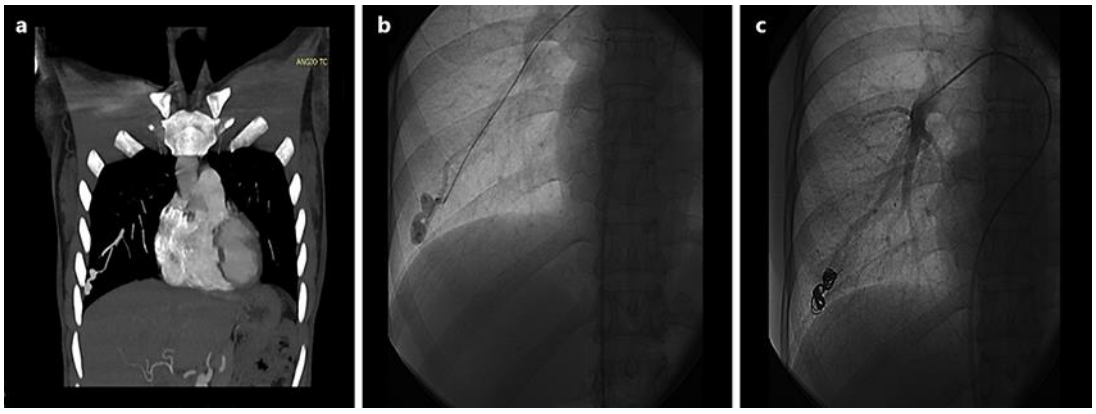

Fig. 2. Thoracic CT angiography and digital subtraction angiography. **a** Thoracic coronal MIP (maximum intensity projection) depicting a simple pulmonary arteriovenous fistula at the middle lobe composed by a small feeding artery, 2 interconnected sinuses, and 1 drainage vein. **b**, **c** Digital angiography before (**b**) and after (**c**) coil embolization. During the contrast injection through the microcatheter (positioned distal on the feeding artery), there is opacification of both the AVF sinuses and the draining vein. After the embolization with 2 detachable microcoils, there is no longer distal opacification proving a total occlusion of the AVF.

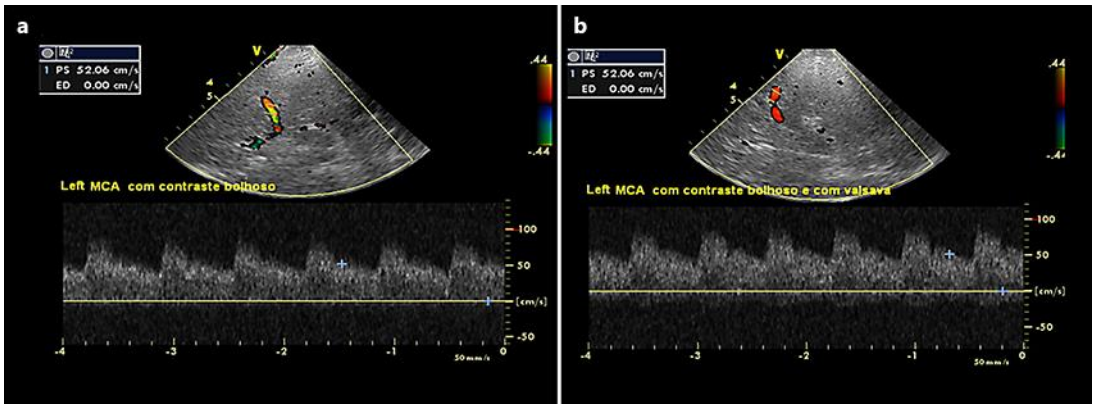

Fig. 3. Transcranial Doppler ultrasonography after PAVF treatment. TCD with microbubble study, 2 months after PAVF treatment, shows no microembolic signals, at rest (**a**) or with Valsalva maneuver (**b**).